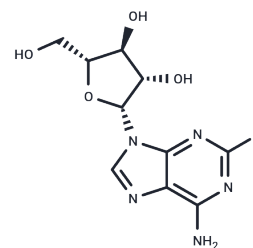


## Fludarabine

## Chemical Properties

CAS No. :	21679-14-1
Formula:	C <sub>10</sub> H <sub>12</sub> FN <sub>5</sub> O <sub>4</sub>
Molecular Weight:	285.23
Appearance:	no data available
Storage:	store at low temperature, keep away from direct sunlight, keep away from moisture Powder: -20°C for 3 years   In solvent: -80°C for 1 year



## Biological Description

Description	Fludarabine (Fludarabinum) is a fluorinated purine analog, an inhibitor of nucleic acid synthesis and an inhibitor of STAT1 activation. Fludarabine has antitumor activity and can be used for the treatment of leukemia and lymphoma.
Targets(IC50)	Apoptosis, Nucleoside Antimetabolite/Analog, STAT, DNA/RNA Synthesis
In vitro	<p><b>METHODS:</b> Multiple myeloma cells RPMI8226, MM.1S and MM.1R were treated with Fludarabine (0-64 µg/mL) for 24-48 h. Cell viability was measured by MTT Assay.</p> <p><b>RESULTS:</b> Fludarabine dose-time-dependently inhibited the proliferation of RPMI8226 cells with an IC<sub>50</sub> of 1.54 µg/mL at 24 h. At 48 h, the IC<sub>50</sub> of Fludarabine on MM.1S and MM.1R cells was 13.48 µg/mL and 33.79 µg/mL, respectively. [1]</p> <p><b>METHODS:</b> Rat aortic VSMCs were treated with Fludarabine (50 µM) and FBS for 30 min, and the expression levels of target proteins were detected by Western Blot.</p> <p><b>RESULTS:</b> FBS stimulation produced progressive JAK2 and STAT-1 activation, and Fludarabine induced a significant reduction in STAT-1 phosphorylation, while it did not alter JAK2 activation. [2]</p>
In vivo	<p><b>METHODS:</b> To assay antitumor activity in vivo, Fludarabine (8-40 mg/kg) was injected intraperitoneally into SCID mice bearing multiple myeloma RPMI8226 once daily for three days.</p> <p><b>RESULTS:</b> The antitumor activity of Fludarabine in vivo was demonstrated by a less than 5-fold increase in tumors treated with 40 mg/kg of Fludarabine over 25 days compared to an approximately 10-fold increase in control tumors. [1]</p> <p><b>METHODS:</b> To study the effect on graft-versus-host disease (GVHD), Fludarabine (0.8 mg/kg) was administered intraperitoneally to (BALB/c x C57BL/6) F1 mice harboring B-cell leukemia (BCL-1) every two weeks for five days in two cycles, followed by intraperitoneal injection of cyclophosphamide (400 mg/kg).</p> <p><b>RESULTS:</b> Mice treated with a Fludarabine-containing regimen prior to transplantation also had much less GVHD clinically and at necropsy, while graft-versus-leukemia appeared to be increased in the same animals. [3]</p>
Cell Research	VSMCs were isolated from the aorta of male Wistar rats weighing ~350-500 g, as previously described. For cell culture experiments, 2 × 10 <sup>5</sup> rat VSMCs were plated in Dulbecco's modified Eagle's medium (DMEM) with 10% fetal bovine serum (FBS). Semiconfluent VSMCs were starved by incubation in 0.5% FBS/DMEM for 36-48 h and then serum-stimulated with normal growth medium (i.e., DMEM containing 10% FBS) in

the presence or absence of fludarabine (50  $\mu$ M) [2].

**Animal Research**

The animals in this study were handled according to the animal welfare regulation of the Magna Graecia University of Catanzaro, and the protocol was approved by the animal use committee of this institution. Fifty Wistar rats weighing  $340 \pm 40$  g were anesthetized with an intramuscular injection of 100 mg/kg ketamine and 5 mg/kg xylazine. Angioplasty of the common carotid artery was performed using a balloon embolectomy catheter, as previously described and well validated in our laboratory. Fludarabine was dissolved in 30% pluronic F127 gel to the final concentrations of 2.5, 5, 15, or 25 mg/ml. At the time of balloon injury, gel containing fludarabine or vehicle was applied around the middle segment (2 cm in length) of the right injured carotid artery (0.1 ml per 1-cm length of the artery segment, equivalent to 0.5, 1, 3, or 5 mg of total fludarabine locally delivered), as previously described. As a control experiment, 200  $\mu$ l of fludarabine/gel solution (25 mg/ml) were applied around the sham-operated carotid artery. To study the fludarabine toxicity, laboratory studies were performed at baseline and 2 wk after drug local delivery (25 mg/ml). Arterial pressure and heart rate were measured indirectly by a tail-cuff plethysmographic technique [2].

**Solubility Information****Solubility**

DMSO: 55 mg/mL (192.83 mM), Sonication is recommended.  
10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2.85 mg/mL (9.99 mM), Solution.  
( $< 1$  mg/ml refers to the product slightly soluble or insoluble)

**Preparing Stock Solutions**

	1mg	5mg	10mg
1 mM	3.5059 mL	17.5297 mL	35.0594 mL
5 mM	0.7012 mL	3.5059 mL	7.0119 mL
10 mM	0.3506 mL	1.753 mL	3.5059 mL
50 mM	0.0701 mL	0.3506 mL	0.7012 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

## Reference

- Meng H, et al. Antitumor activity of fludarabine against human multiple myeloma in vitro and in vivo. *Eur J Haematol.* 2007 Dec;79(6):486-93.
- Yang L, Li N, Yang D, et al. CCL2 regulation of MST1-mTOR-STAT1 signaling axis controls BCR signaling and B-cell differentiation. *Cell Death & Differentiation.* 2021: 1-18
- Zhang J, Guo H, Wang L, et al. Cediranib enhances the transcription of MHC-I by upregulating IRF-1. *Biochemical Pharmacology.* 2024: 116036.
- Lu X, Ji Q, Pan H, et al. IL-23p19 deficiency reduces M1 macrophage polarization and improves stress-induced cardiac remodeling by alleviating macrophage ferroptosis in mice. *Biochemical Pharmacology.* 2024: 116072.
- Zeng L, Lyu X, Yuan J, et al. STMN1 Promotes Tumor Metastasis in Non-small Cell Lung Cancer Through Microtubule-dependent And Nonmicrotubule-dependent Pathways. *International Journal of Biological Sciences.* 2024, 20(4): 1509.
- Torella D, et al. Fludarabine prevents smooth muscle proliferation in vitro and neointimal hyperplasia in vivo through specific inhibition of STAT-1 activation. *Am J Physiol Heart Circ Physiol.* 2007 Jun;292(6):H2935-43.
- Wang X, Li X, Wang J, et al. SMGL-1/NBAS acts as a RAB-8 GEF to regulate unconventional protein secretion. *Journal of Cell Biology.* 2022, 221(7): e202111125
- Zhang T, Wang Y, Li Q, et al. Mesenchymal stromal cells equipped by IFN $\alpha$  empower T cells with potent anti-tumor immunity. *Oncogene.* 2022: 1-16.
- Weiss L, et al. Fludarabine in combination with cyclophosphamide decreases incidence of GVHD and maintains effective graft-versus-leukemia effect after allogeneic stem cell transplantation in murine lymphocytic leukemia. *Bone Marrow Transplant.* 2003 Jan;31(1):11-5.
- Zhu Y, Gu H, Yang L, et al. Involvement of MST1/mTORC1/STAT1 activity in the regulation of B-cell receptor signalling by chemokine receptor 2. *Clinical and Translational Medicine.* 2022, 12(7): e887.
- Zhu Y, Gu H, Yang L, et al. The sequential role of Mst1/mTORC1/STAT1 activity in chemokine receptor 2-regulated B cell receptor signaling[J]. *Authorea Preprints.* 2021
- Wang S, He F, Li Z, et al. Long non-coding RNA BANCRC promotes interferon- $\beta$ -induced cardiomyocyte apoptosis by targeting signal transducer and activator of transcription 1 in vitro[J]. *International Journal of Clinical and Experimental Pathology.* 2020, 13(11): 2840.
- Chen C, Lu M, Lin S, et al. The nuclear gene rpl18 regulates erythroid maturation via JAK2-STAT3 signaling in zebrafish model of Diamond-Blackfan anemia. *Cell Death & Disease.* 2020, 11(2): 1-11
- Chu K H, Lin S Y, Chiang B L. STAT6 Pathway Is Critical for the Induction and Function of Regulatory T Cells Induced by Mucosal B Cells. *Frontiers in immunology.* 2021 Jan 29;11:615868. doi: 10.3389/fimmu.2020.615868. eCollection 2020.
- Chu K H, Lin S Y, Chiang B L. STAT6 Pathway Is Critical for the Induction and Function of Regulatory T Cells Induced by Mucosal B Cells[J]. *Frontiers in immunology.* 2020, 11.
- Wang S, He F, Li Z, et al. Long non-coding RNA BANCRC promotes interferon- $\beta$ -induced cardiomyocyte apoptosis by targeting signal transducer and activator of transcription 1 in vitro. *International Journal of Clinical and Experimental Pathology.* 2020, 13(11): 2840.
- Chen C, Lu M, Lin S, et al. The nuclear gene rpl18 regulates erythroid maturation via JAK2-STAT3 signaling in zebrafish model of Diamond-Blackfan anemia[J]. *Cell Death & Disease.* 2020, 11(2): 1-11.
- Ye S, Li S, Qin L, et al. GBP2 promotes clear cell renal cell carcinoma progression through immune infiltration and regulation of PD-L1 expression via STAT1 signaling. *Oncology Reports.* 2023, 49(3): 1-14.
- Yang L, Li N, Yang D, et al. CCL2 regulation of MST1-mTOR-STAT1 signaling axis controls BCR signaling and B-cell differentiation[J]. *Cell Death & Differentiation.* 2021: 1-18.
- Zhang X, Wang J, Wang M, et al. IFN- $\beta$  Pretreatment Alleviates Allogeneic Renal Tubular Epithelial Cell-Induced NK Cell Responses via the IRF7/HLA-E/NKG2A Axis. *The Journal of Immunology.* 2023

**Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins**

**This product is for Research Use Only · Not for Human or Veterinary or Therapeutic Use**

Tel: 781-999-4286    E\_mail: info@targetmol.com    Address: 36 Washington Street, Wellesley Hills, MA 02481